

REMARKS

The present application provides, *inter alia*, particle-forming compositions of modafinil compounds and related methods of preparing such compositions. The application also provides methods of using these compositions to treat a broad range of serious ailments, including, *e.g.*, stroke, Parkinson's disease, eating disorders, attention deficit hyperactivity disorder, and sleep apnea.

Claims 1, 3, 4, 8-13, 15-43, 45-50, 55-60, and 63-66 are pending in this application. These claims stand finally rejected as allegedly obvious under 35 U.S.C. § 103 in view of various prior art references. As explained below, the pending claims are in condition for allowance and that the rejections should be reconsidered and withdrawn.

I. The Rejections Under 35 U.S.C. § 103 Should be Withdrawn

A. Legal Standard

To establish a *prima facie* case of obviousness, there must be a clearly articulated reason or rationale, either in the prior art itself or in the knowledge generally available to one of ordinary skill in the art, why the claimed invention is obvious in light of a reference or combined reference teachings. MPEP §§ 2143, 2143.01; *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1739-43 (2007). There must also be a reasonable expectation of success. MPEP § 2143.02. Further, the prior art combination must address all of the elements of the claim at issue. MPEP § 2143.03. The rationale to make the claimed combination and the reasonable expectation of success must be found in the prior art and cannot be based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991). References that teach away from the claimed invention and references that teach away from their combination cannot support a *prima facie* case of obviousness. MPEP § 2145.X.D.

In determining the differences between the prior art and the claims, the question under 35 U.S.C. § 103 is **not** whether the differences **themselves** would have been obvious. Instead, the relevant inquiry is whether the **claimed invention as a whole** would have been obvious. MPEP § 2141.02.I (citing *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530 (Fed. Cir. 1983) and *Schenck v. Nortron Corp.*, 713 F.2d 782 (Fed. Cir. 1983)).

B. Discussion

Applicants' independent claim 1 recites, *inter alia*:

"A **non-aqueous, liquid solution** comprising a modafinil compound . . . characterized in that the solution **spontaneously forms** an aqueous, liquid, homogeneous, stable **composition of non-crystalline particles when contacted with an aqueous medium**" (emphasis added).

As set forth below, the various combinations of references cited in the office action teach away from the claimed invention, teach away from their combination, and fail to address every element of Applicants' claim. Moreover, rather than considering the claimed invention as a whole, the office action has engaged in impermissible hindsight, piecing together teachings of the prior art using Applicants' specification as a blueprint to address individual claim limitations. MPEP § 2142.02.I. But because the office action must consider the invention as a whole, *Stratoflex*, 713 F.2d at 1537, this piecemeal approach is improper.

1. The Rejections Under Nguyen and Esteve Should be Withdrawn

Claims 1, 3, 4, 8-13, 15, 17-35, 45-47, 55, 59, 63, and 66 stand rejected as allegedly obvious over Nguyen (U.S. 5,843,347) ("Nguyen") in view of Esteve (U.S. 6,566,404) ("Esteve") (office action at paragraphs 3-11). Because Nguyen and Esteve – in combination¹ – do not address every element of applicants' claim and teach away from the claimed invention, the prior art cannot support a *prima facie* case of obviousness, and the rejections should be withdrawn.

The pending claims recite, *inter alia*, liquid solutions. But because Nguyen and Esteve teach away from the claimed invention and from combination with one another, the cited references cannot support a *prima facie* case of obviousness. MPEP § 2145.X.D. As the office action concedes, "Nguyen **does not teach a liquid composition**" (office action at paragraph 4). Applicants submit that not only does Nguyen fail to teach a liquid composition, but the reference in fact **teaches away** from such compositions.

¹ The office action alleges that applicants' prior response addressed Nguyen and Esteve individually and did not address the combination of those references. Applicants respectfully draw attention to pages 4 and 5 of their Nov. 25, 2008 response, wherein applicants explained that because Nguyen did not address every element of the cited claims and "**the addition** of Esteve does not cure Nguyen's deficiency," "**the Nguyen-Esteve combination** fails to make out a *prima facie* case of obviousness" (emphasis added).

a. Nguyen Cannot Support the Obviousness Rejections Because It Fails To Address Multiple Elements Of Applicants' Claims

A careful review of Nguyen is necessary to properly frame the failure of the Nguyen-Esteve combination to support a *prima facie* case of obviousness. Nguyen is directed toward formation of lyophilized, freeze-dried particles, which are essentially free of liquid. *See* Nguyen at col. 5, lines 10-15 (forming dried particles by freeze-drying composition); *see also* CONCISE CHEMICAL AND TECHNICAL DICTIONARY 719 (1986) (attached as **Exhibit A** hereto) (defining lyophilization as **dehydrating** a frozen material under vacuum). Because Applicants' claims expressly recite **liquid** solutions, one of skill in the art would not begin with Nguyen's inherently **dehydrated** compositions to arrive at Applicants' claimed **liquid** solutions. MPEP § 2143.03 (prior art must address every element of claims at issue to support *prima facie* case of obviousness).

To the extent the pending rejections are based on Nguyen's alleged disclosure of compositions containing an active ingredient and a surfactant (*see* office action at paragraphs 4, 7), these compositions are **not** liquid, as the office action concedes (*see* office action at paragraph 4, "Nguyen does not teach a liquid composition"). Instead, the Nguyen compositions are "**pasty**" (*i.e.*, viscous), in order that they can be extruded to give rise to the final particulate product (*see* Nguyen at col. 5, lines 3-11 and claim 1). This extrusion, however, could not be performed if the compositions were **liquid**, as are Applicants' compositions (*see* pending claim 1). Thus, because liquid compositions are fundamentally incompatible with the "pasty mixture[s]" of Nguyen and the extrusion of these pasty mixtures, Nguyen in fact teaches away from the **liquid** solutions of the present invention and accordingly cannot support a *prima facie* case of obviousness. *See* MPEP § 2145.X.D (reference that teaches away from claimed invention cannot support *prima facie* obviousness); *see also* MPEP § 2143.01.V (no *prima facie* case of obviousness if proposed modification to prior art would render prior art "unsatisfactory" for its intended purpose).

Nguyen also fails to address all elements of Applicants' claims for another reason. While the office action suggests that the lyophilized preparation of Nguyen meets the "non-aqueous" element of Applicants' claims, the non-aqueous compositions of Nguyen are in fact freeze-dried, lyophilized microbeads (*see* Nguyen at, e.g., col. 7, lines 45-48), that are

qualitatively different from the liquid solutions recited by Applicants' claims. Accordingly, Nguyen thus fails to disclose compositions that are simultaneously "liquid" and "non-aqueous," and for this additional reason, Nguyen cannot support a *prima facie* case of obviousness.

b. Because Esteve Does Not Cure Nguyen's Deficiencies, the Nguyen-Esteve Combination Cannot Support A *Prima Facie* Case Of Obviousness

Implicitly recognizing that the Nguyen reference cannot by itself establish a *prima facie* case of obviousness against the pending claims, the office action alleges that adding Esteve to Nguyen cures Nguyen's deficiencies. But the Nguyen-Esteve combination also fails to support a *prima facie* case of obviousness against the cited claims.

The previous office action relied on Esteve for that reference's alleged disclosure of modafinil as a liquid formulation (*see* Sept. 30, 2008 office action at paragraph 5). But Esteve's disclosure of liquid-form modafinil does not cure Nguyen's deficiencies. While Esteve discloses liquid-form modafinil, liquid-form modafinil remains incompatible with Nguyen's requirement that the active ingredient-surfactant composition be "pasty" (*i.e.*, viscous) so as to enable the user to extrude and then freeze-dry the composition. In fact, Nguyen – as discussed above – **teaches away** from liquid preparations, because liquid preparations are incompatible with Nguyen's requirement that the active ingredients be present as "pasty," extrudable mixtures. *See* MPEP § 2143.01.V (proposed combination of references cannot render prior art "unsatisfactory" for its intended purpose). Accordingly, the Nguyen-Esteve combination is improper on its face.

Moreover, even if one of ordinary skill in the art were motivated to somehow combine the teachings of Nguyen and Esteve, neither reference, either alone or in combination, describes a ***non-aqueous solution*** comprising a modafinil compound, an organic solvent and a surfactant, as recited in the instant claims. Nguyen, for example, describes, as a first step, a ***mixture*** of an active ingredient with a polymer having a molecular weight greater than 10,000 daltons, and a dispersible component such as lactose, glycerol, mannitol, glucose, sucrose, maltodextrin and cyclodextrins (Nguyen at col 5, lines 3 to 5, col. 6, lines 1-3 and col. 6, lines 45-46). While the prior art and the claimed invention both cite modafinil, the office action nonetheless fails to explain why one of skill in the art would be

motivated to prepare the *non-aqueous solutions* of the claimed invention based on the prior art's other, different ingredients. *Cf.* MPEP § 2141.02.I (obviousness inquiry focuses on invention as a whole, not on individual differences between prior art and claimed invention).

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In sum, (1) Nguyen fails to address both the “liquid” and “non-aqueous” elements of the cited claims; (2) Nguyen teaches away from the cited claims; (3) Nguyen teaches away from combination with Esteve; and (4) the addition of Esteve does not in any event cure Nguyen's deficiencies or result in the claimed *non-aqueous solutions*. Accordingly, the cited prior art fails to support a *prima facie* case of obviousness against the cited claims and all rejections should be withdrawn.

2. The Rejections Under Nguyen and Shah or Nguyen and Charman Should be Withdrawn

As discussed above, Nguyen both fails to address every element of Applicants' claims **and** teaches away from the claims. Claims 1, 3, 4, 8-13, 15, 17-35, 45-47, 48-50,² 55, 59, 63, and 66 stand rejected over Nguyen in further view of Shah or Charman (office action at paragraphs 12, 13, and 17). But the addition of either Shah or Charman does not cure Nguyen's shortcomings.

As discussed in Applicants' Nov. 25, 2008 response, Shah and Charman are both directed toward delivery of **lipophilic compounds** (Shah at page 15; Charman at page 87). But because modafinil is **poorly soluble** in lipids (see pending application at [0006] and U.S. 6,489,363 at col. 1, lines 56-59), one of skill in the art would **not** look to either Shah or Charman to deliver modafinil because there would no expectation of success. Put another way, Shah and Charman are directed toward delivery of compounds with solubility characteristics that are **opposite** of the solubility characteristics of modafinil. *See* MPEP

² While the pending office action suggests that “Applicant has not argued against the [] rejections of claims 48-50” (office action at paragraph 17), Applicants respectfully draw attention to page 7 of their November 25, 2008 response: “because claim 1 is nonobvious [over Nguyen/Shah], **all claims that depend from claim 1 are also nonobvious** and the rejection of those claims should be withdrawn” (emphasis added). Accordingly, Applicants respectfully submit that they have argued against the previous rejections of claims 48-50, all of which depend from claim 1. (In any event, given that Applicants listed all rejected claims except for claims 48-50 in the relevant section of the November 25 response, it is apparent that any failure to specifically enumerate claims 48-50 is no more than an oversight.)

§ 2143.02.II (no *prima facie* case of obviousness where no expectation that prior art would successfully arrive at claimed invention). For this reason, the combination of Shah or Charman with Nguyen cannot support a *prima facie* case of obviousness.

Further, even if combining Nguyen with Shah or Charman were proper, the resulting composition would be freeze-dried particles comprising a **lipophilic** active ingredient. But such compositions do not address applicants' claimed compositions, which compositions include, *inter alia*, modafinil, which is – as discussed – **poorly soluble** in lipids (see pending application at paragraph [0006]). Hence, even if combining Nguyen with Shah or Charman were proper, the resulting composition does not address every element of Applicants' claims. Accordingly, the combination cannot support a *prima facie* case of obviousness. See MPEP § 2143.03 (prior art must address all elements of claim in order to make out *prima facie* case of obviousness). Because (1) combining Nguyen with Shah or Charman combination is improper and (2) combining Nguyen with Shah or Charman combination would not in any event address every element of Applicants' claims, all rejections over the Nguyen-Shah or Nguyen-Charman combination should be reconsidered and withdrawn.

3. The Rejections Under Nguyen and Grebow Should be Withdrawn

Claims 1, 3, 4, 8-13, 15, 17-35, 45-50, 55, 59, 63, and 66 stand rejected over Nguyen in view of Grebow (U.S. 5,618,845) (office action at paragraph 18). These rejections should be reconsidered and withdrawn.

As discussed above, Nguyen fails to address every element of Applicants' claims **and** teaches away from the claims. The addition of Grebow does not cure Nguyen's deficiencies. While Grebow teaches suspensions of modafinil particles (Grebow at col. 8, line 22), the only disclosed suspensions are made in **deionized water** and are therefore contrary to both the "non-aqueous" and "solution" elements of Applicants' claims and to the freeze-dried compositions set forth in Nguyen. See MPEP § 2145.X.D (references that teach away from their combination or from the claimed invention cannot support a *prima facie* case of obviousness).

Moreover, given that Grebow discloses suspensions of modafinil particles, one of skill would have no reason to begin with Grebow to arrive at the claimed invention. As set forth in pending claim 1, the claimed invention discloses **precursor solutions** used to produce modafinil particle suspensions. By contrast Grebow discloses **modafinil particle**

suspensions, and one of skill in the art would have no reason to modify the desired modafinil particle suspension to arrive at the **precursor** to that suspension. Finally even if Nguyen were combined with Grebow, the resulting combination would disclose **aqueous** particle suspensions, which is contrary to the “**non-aqueous**” and “**solution**” elements of the cited claims. Accordingly, because Nguyen and Grebow teach away from their combination and away from the cited claims, all rejections based on those references should be withdrawn.

4. The Rejections Over Nguyen, Grebow, and Hochlowski Should be Reconsidered and Withdrawn

Claims 1, 15, and 16 stand rejected over Nguyen in view of Grebow and Hochlowski (U.S. 5,589,485) (*see* office action at paragraph 22). These rejections should be reconsidered and withdrawn.

As discussed above, Nguyen and Grebow teach away from both the claimed invention and from their combination, and, fail to address every element of the pending claims. The addition of Hochlowski does not remedy the shortcomings of Nguyen and Grebow because Hochlowski merely discloses a few pharmaceutically-acceptable diluents useful in liquid formulations (Hochlowski at col. 5, lines 35-43), and does not address a “non-aqueous, liquid solution comprising a modafinil compound . . . characterized in that the solution spontaneously forms an aqueous, liquid, homogeneous, stable composition of non-crystalline particles when contacted with an aqueous medium.” Accordingly, the addition of Hochlowski to Nguyen and Grebow does not cure those references’ deficiencies, and all rejections under this reference combination should be reconsidered and withdrawn.

II. Conclusion

For all of the foregoing reasons, Applicants submit that the pending claims are allowable over the cited references and that the rejections of the pending claims under 35 U.S.C. § 103(a) should be withdrawn. Accordingly, Applicants respectfully request that the Examiner reconsider the pending rejections and pass the pending claims to allowance.

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PATENT

If the Examiner believes that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided. Favorable consideration and an early notice of allowance are respectfully requested.

Respectfully submitted,

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